A COMPARATIVE EVALUATION OF EFFICACY AND TOLERABILITY OF FIXED DRUG COMBINATION OF BRIMONIDINE AND TIMOLOL WITH TIMOLOL MONOTHERAPY IN PATIENTS WITH PRIMARY OPEN-ANGLE GLAUCOMA: AN OPEN LABELED PROSPECTIVE STUDY

Abstract

Background:

Glaucoma, an optic neuropathy, is a worldwide leading cause of visual impairment and blindness. It is a neurodegenerative disease associated with loss of Retinal Ganglion Cells and a raised intraocular pressure (IOP) which is the modifiable risk factor for glaucoma. It is an important cause of blindness in the developing world and a major health burden in the developed world. Primary open angle glaucoma (POAG) is characterized by chronically elevated IOP with optic neuropathy and the cause is unknown for the elevated IOP. Reduction of IOP with less complications or adverse effects remains the mainstay therapy for the first-line treatment of glaucoma. Two or more medications are needed to reach a target IOP to arrest further visual loss in many patients with POAG. The drugs commonly used to reduce IOP in glaucoma include topical prostaglandin analogues like bimatoprost, beta-blockers like timolol, alpha-agonists like brimonidine, carbonic anhydrase inhibitors like dorzolamide, and parasympathomimetics. Fixed drug combinations have been approved for treatment of glaucoma. The available fixed combination drugs in the market are timolol 0.5% combined with bimatoprost, dorzolamide or brimonidine. Neuroprotection approach

prevents neuronal injury or promotes neuronal recovery and protects the RGC from glaucomatous injuries. This study is undertaken with the aim to compare and evaluate the efficacy and safety of a fixed drug combination of 0.2% brimonidine and 0.5% timolol with the effect of 0.5% timolol administered as monotherapy in patients with POAG.

Objective

To study the Intra Ocular Pressure lowering effect of fixed dose combination of Brimonidine-Timolol with Timolol monotherapy in patients with Primary Open-Angle Glaucoma and to assess the effects of fixed dose combination of Brimonidine-Timolol on visual acuity and visual field changes.

Methods

Single centre, prospective, open label, parallel group, comparative study conducted for a period of 12 weeks at Ophthalmology department, Govt. Stanley Medical College and Hospital, Chennai-1. The study was commenced after obtaining approval from the Institutional Ethics Committee. Patients with Primary Open Angle Glaucoma were screened by detailed medical history and ocular examination. A total of 60 patients satisfying the selection criteria were included in the study. After getting informed consent they were randomized into 2 groups. Group A and Group B. Each group consisting of 30 patients. Group A patients [Test group]: Fixed dose combination of Brimonidine-Timolol eye drop instilled twice daily. Group B patients: Timolol 0.5% eye drop instilled twice daily. After enrollment into the study and initiation of the study drugs, the

follow-up was done after 2 weeks, 4 weeks, 8 weeks and 12 weeks. After 12 weeks of study period the patients were followed up in the Ophthalmology department. The primary efficacy end point was the change from baseline intraocular pressure to the target pressure. Safety was assessed in terms of ocular and systemic adverse effects both subjective and objective.

Results

Both timolol monotherapy and brimonidine-timolol fixed drug combination are effective agents in reducing intraocular pressure throughout the study period when measured at 2^{nd}, 4^{th}, 8^{th} and 12^{th} weeks. When efficacy of brimonidine-timolol fixed combination was compared with timolol monotherapy, brimonidine-timolol fixed combination was more effective in reducing IOP compared to timolol alone. Comparing to timolol group, mean IOP was markedly reduced in FDC BT group at the end of treatment, $p<0.05$. There was no significant changes in CCT, visual field changes and vital parameters. Comparing to Timolol group, patients in FDC BT group had less side effects. There was no serious adverse effects noted in both groups.

Conclusion

In our study both Fixed drug dose combination of Brimonidine-Timolol and Timolol monotherapy have been shown to be efficacious in POAG. Compared to Timolol monotherapy, FDC Brimonidine-Timolol therapy has shown a more significant reduction in IOP. Moreover, FDC Brimonidine-Timolol therapy was found to have produced less

number of side effects in comparison. Thus based on the results of our study, it can be concluded that brimonidine-timolol fixed combination is more effective and safer in lowering IOP in comparison to Timolol monotherapy for the treatment of primary open angle glaucoma. In addition, the neuroprotective effects of brimonidine, could prove to be beneficial on arresting the progression of the disease on long term.

Keywords

Primary open angle glaucoma (POAG), Intraocular pressure (IOP), Timolol, Fixed dose brimonidine-timolol, Neuroprotection, visual field.